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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of

Hans SIGRIST et al.

On Appeal from: 1623

Serial No.: 09/606,040

Filed: June 29, 2000

For: PROCESS FOR THE MODIFICATION OF SURFACES

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PARKHURST & WENDEL

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this Brief.

Respectfully submitted,

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Date: May 13, 2003

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re patent Application of

Hans SIGRIST et al.

Group Art Unit: 1634

Serial No.: 09/606,040

Examiner: Arun K. Chakrabarti

Filed: June 29, 2000

For: PROCESS FOR THE MODIFICATION OF SURFACES

BRIEF ON APPEAL

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I. REAL PARTY IN INTEREST

The real party in interest is Centre Suisse d'Electronique et de Mirotechnique S.A., whose ownership interest is shown in an Assignment recorded at Reel 011754, Frame 0210 on October 24, 2000.

II. RELATED APPEALS AND INTERFERENCES

There is no appeal or interference known to appellants, their assignee, or the undersigned that would directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

The application was filed with fifteen claims. Restriction was required among three claim groups, namely claims 1 to 11, claims 12 and 13, and claims 14 and 15. Appellants elected to prosecute claims 1 to 11. Claims 3, 5 to 12, and 15 were amended in a Preliminary Amendment filed contemporaneously with the case and claims 3, 5, and 7 were further amended and claims 16 to 20 were added in an Amendment Under 37 CFR 1.111 filed February 28, 2002. The claims in the case thus are claims 1 to 20; claims 1 to 11 and 16 to 20 having been examined and finally rejected are

before the Board while claims 12 to 15 stand withdrawn from consideration.

IV. STATUS OF AMENDMENTS

A Request for Reconsideration was filed in reply to the Final Rejection. There is no requested change to the claims pending entry or review. The claims on appeal in Appendix A to this Brief are the claims that were finally rejected.

V. SUMMARY OF INVENTION

The present invention is directed to a process that facilitates preparation of a carbohydrate structure on a material (usually solid; see the first two paragraphs on page 6) surface by photochemically fixing at least a compound of the formula (1a) shown in Fig. 1 wherein X is a mono- or oligo-saccharide radical or photochemically fixing a related compound wherein ZH groups are subsequently converted to ZX moieties wherein X is a mono- or oligo-saccharide radical and then enzymatically attaching at least one further carbohydrate to the X radicals of the modified surface obtained in the first step of the process. Thus, the second step of the process involves attaching carbohydrates enzymatically to

the mono-or oligo-saccharide radical(s) fixed on the material surface.

The process is particularly effective in permitting a variety of carbohydrates to be attached to a solid material surface. The invention is especially useful in treating biomedical articles or biosensors to provide modified surfaces thereon; see page 1, first two paragraphs.

VI. ISSUE

The sole issue for consideration by the Board is whether the subject matter of claims 1 to 11 and 16 to 20 patentably defines in the sense of 35 USC 103 over Miyasaka et al. U.S. 5,154,808 in view of Mazid et al. U.S. 5,308,460.

VII. GROUPING OF CLAIMS

For purposes of the present appeal, claims 1 to 11 and 16 to 20 may be considered as a group.

VIII. ARGUMENT

The references in combination do not teach or suggest the instant invention because the references themselves are not directed to similar subject matter. The secondary reference in no proper manner teaches or suggests the modification/further treatment of the primary reference technique needed to practice the invention of this case.

The claims on appeal are directed to a method for preparing a carbohydrate substrate on a material substrate wherein, following photochemical fixation of a mono- or oligosaccharide-containing material of formulae (1a) and (1b) of claim 1, at least one further carbohydrate is enzymatically attached to the X radicals of the modified surface attained according to the photochemical fixation steps (a₁) or (a₂).

The Examiner asserts that the primary reference teaches a photochemical fixing of at least one compound onto a material surface in carbohydrate preparation where the fixation is undertaken using azide electron withdrawing groups. The Examiner acknowledges in the last paragraph on page 3 of the Final Rejection that the primary reference does not teach a process for enzymatic attachment of at least one further carbohydrate to the X radicals

of a modified surface (steps (a₁) and (a₂) of claim 1). Mazid et al. '460 is said to supply the teaching necessary to make the claimed subject matter obvious to the person of ordinary skill in the art. Appellants emphatically disagree.

The first full paragraph of page 3 of the Final Rejection contains the statement that Miyasaka et al. '808 teaches techniques for the preparation of a carbohydrate on a material surface by photochemically fixing one or more different compounds onto the material surfaces. The Examiner cites column 2, line 39 to column 6, line 38 and claims 1 and 2 of the patent in support of his position. The Examiner has not identified in the reference any compound corresponding to the compound of the formula 1a in appellants' claim 1.

The Board, moreover, will note that "carbohydrate" is nowhere mentioned in any of the sections of Miyasaka et al. '808 cited by the Examiner. Indeed, the reference discusses the immobilization of proteins (carbohydrates are not proteins) by substantially water-insoluble (carbohydrates are highly water-soluble) nitrene or carbene precursors. See, as a representative matter, claim 1 of the patent. Such precursors are not immobilized on the surface but rather are dissolved in an organic thin film before exposure to

light. See column 8, lines 35 to 43. Those precursors have to be substantially water-insoluble to avoid diffusion out of the organic thin film layer during the protein adsorption process. The Board is directed to the reaction scheme shown in the top of enclosed Appendix B. (This paper was filed with the Request For Reconsideration filed February 4, 2003.) The reaction scheme depicted in the top of Appendix B is the Miyasaka et al. '808 reaction scheme. This prior art technique does not direct the artisan to the present invention which concerns preparing a carbohydrate substrate on a material in a particular fashion. The artisan is not directed to the process of appellants.

It is asserted also at page 3 of the Final Rejection that Miyasaka et al. '808 patent claim 13, fifth paragraph, teaches a process wherein X is a disaccharide radical. Appellants say nowhere in the text or the chemical structures in claim 13 is there any indication of or reference to a disaccharide. The compounds listed in patent claim 13 are representative nitrene and carbene precursors used in the patent method. Miyasaka et al. '808 indicates also that the precursors must be substantially water-insoluble; see the paragraph above.

Accordingly, Miyasaka et al. '808 does not teach a process of photochemically attaching carbohydrates to organic thin film material, and as acknowledged on page 3, next-to-last paragraph, of the Final Rejection, the reference does not teach a process of enzymatically attaching one or more carbohydrates to the modified surface. The primary reference describes a technique that is totally different from the claimed invention.

Mazid et al. '460 does not supply what is missing from the primary reference teaching. (Nor is there any proper reason to combine these teachings). Miyasaka et al. '808, as explained above, does not teach photochemical fixation of mono- or oligo-saccharide-containing compounds to a material surface. Mazid et al. '460 describes oligosaccharide production using enzymes, including carbohydrate modifying enzymes that are immobilized on a material surface. The technique is generally understood to be solid phase carbohydrate synthesis with immobilized enzymes. And, of course, as mentioned above, Miyasaka et al. '808 does not relate to carbohydrates or disaccharides. Thus, there is no proper reason to combine these references. The Board is directed to the second reaction scheme depicted in Appendix B; that reaction scheme is that of Mazid et al. '460.

Appellants strongly dispute that Mazid et al. '460 in the Abstract, col. 2, working examples, and claims "teach a process of attaching enzymatically one or more further carbohydrates to the X radicals of the modified surface [presumably as shown in Miyasaka et al '808]." In the first instance, the primary reference does not teach "X radicals" (as defined by appellants) on a "modified surface."

The secondary reference does not properly teach or suggest the asserted modification of the primary reference teaching because Mazid et al. '460 describes using enzymes, including carbohydrate-modifying enzymes that are immobilized at a material surface, acting on mono- and oligo saccharides. (Please refer to Appendix B.) The enzyme substrate, e.g., a carbohydrate entity to be modified by carbohydrate-modifying enzymes, is presented in a soluble rather than in an immobilized form. The working examples of the reference show that the immobilized enzyme is a material facilitating oligosaccharide formation. The reference doesn't teach or suggest enzymatic attachment of at least one carbohydrate to the mono- or oligosaccharide radical of a material formed in step (a₁) or (a₂) of instant claim 1.

The present invention, in contrast to the Mazid et al. '460 technique, is directed to a process where, in one aspect, a diazirine-modified carbohydrate can be fixed by photochemical means to a material substrate which, unlike the primary reference, does not present carbene-generating entities at the surface. The carbene-generating molecular entity is a part of the carbohydrate substrate. The present invention also shows for the first time that the surface-immobilized enzyme substrates are recognized as enzyme substrates by carbohydrate-modifying enzymes such as glycosyltransferases. Upon photochemical attachment of diazirine-labeled carbohydrates, the carbohydrate portion remains structurally intact and can be recognized as an enzyme substrate by the carbohydrate-modifying enzymes. The Board is directed to the third reaction scheme depicted in Appendix B showing the instantly claimed process.

If the enzyme substrates are presented directly to a photochemically-active material surface as described by the Examiner, the carbohydrate substrate would be covalently bound to the surface through chemical functional groups of the carbohydrate substrate (the OH functions of the carbohydrate molecule) that are

essential for enzyme recognition. The carbohydrate-modifying enzymes cannot catalyze the specific reactions.

Moreover, in contrast to the techniques of the primary and secondary references, the instantly claimed process involves photochemically attaching carbohydrates carrying carbene precursor functions to material surfaces. The product of the photochemical immobilization step of the present invention is a carbohydrate-modified surface that exposes the intact carbohydrate structure to the aqueous medium. (Please refer to Appendix B.) Carbohydrate-modifying enzymes can subsequently be used to modify the initiated carbohydrate chain, which can be referred to as solid phase carbohydrate synthesis with immobilized carbohydrate (enzyme) substrates.

The differences among and between the techniques of the primary and secondary references and the instantly claimed process are depicted in the sheet attached as Appendix B. The document establishes that the technologies of the primary and secondary references are dissimilar and there is no proper reason to combine them for any purpose and especially not for a teaching or suggestion of the present invention.

The Advisory Action contained three points in support of the rejection. Appellants address those points seriatim.

A) Appellants were said merely to argue the references individually. Not so. Both the primary and secondary references were discussed and appellants explained why, due to the dissimilar nature of the teachings of those references, they could not properly be combined to meet the features of the present claims. Indeed, the references could not properly be combined for any reason. Moreover, appellants submitted Appendix B showing the differences among and between the Miyasaka et al. '808 teachings, the Mazid et al. '460 teachings, and the claimed invention. However, the record contains no comment by the Examiner with respect to that document. The references were not argued merely individually.

B) It is asserted that appellants merely "recognized another advantage" that "would flow naturally from following the suggestion of the prior art." Appellants have detailedly shown above that it is not proper to combine Miyasaka et al. '808 and Mazid et al. '460. There is no other advantage flowing "naturally from following the suggestion of the prior art" because the prior art does not lead the artisan to the present invention.

C) Appellants argue that Miyasaka et al. '808 does not teach the carbohydrate structure of the claims. The Examiner states that column 5, line 5, and column 6, line 15, of Miyasaka et al. '808 show mono-or oligo saccharide structures but the comment is incorrect and does not contradict appellants' statement about carbohydrate structure. Saccharides in general have a common basic element: $(\text{HCOH})_x$ which is repeated x fold. For example, the formula of the simplest monosaccharide glucose is $\text{C}_6\text{H}_{12}\text{O}_6$. The formulae mentioned in column 5, line 5 and column 6, line 15 are not saccharides. There are simply not sufficient oxygen atoms (O) in the formula given. The compounds shown in column 5, line 5 and column 6, line 15 of the primary reference refer to hydrophobic photoreagents that are esterified alkanes.

Lastly, it was asserted that the use of "comprising" in the claims opened them to additional steps or compounds "which may modify the carbohydrate structure." Appellants say "comprising" does not and cannot convert alkanes into saccharides. We are dealing with chemistry, not metaphysics.

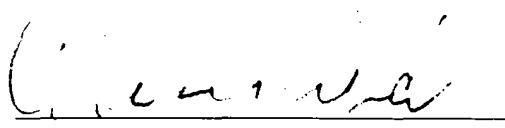
IX. CONCLUSION

For the foregoing reasons, claims 1 to 11 and 16 to 20 patentably define over the cited art and the Board is asked to reverse the Examiner and so hold.

Respectfully submitted,

PARKHURST & WENDEL, L.L.P.


Date


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Registration No. 24,453

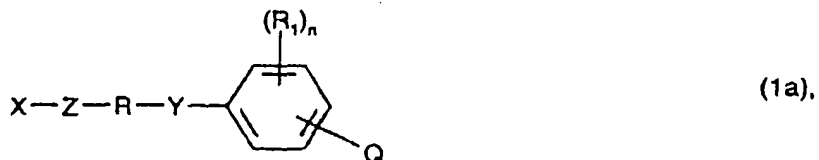
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APPENDIX A

THE CLAIMS ON APPEAL

1. A process for the preparation of a carbohydrate structure on a material surface comprising the steps of:

(a₁) photochemically fixing one or more different compounds of formula



onto the material surface,

wherein X is the radical of a mono- or oligosaccharide,

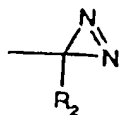
R is a divalent organic radical having from 2 to 30 C-atoms which may be further substituted,

Z is -O-, -S- or a direct bond,

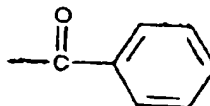
Y is a functional group linking R to the aromatic ring,

R₁ is an electron-withdrawing substituent and n is an integer from 0 to 4,

Q is a radical of formula



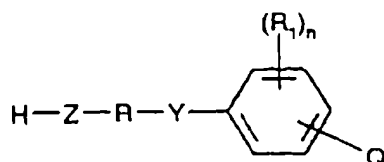
(2a) or



(2b)

and R_2 is an electron-withdrawing substituent; or

(a₂) photochemically fixing a compound of formula



wherein R , R_1 , n , Y , Z and Q are as defined above, onto the material surface and subsequently converting the $-\text{ZH}$ groups to $-\text{Z}-\text{X}$ moieties, wherein X has the above meaning; and

(b) enzymatically attaching one or more further carbohydrates to the X radicals of the modified surface obtained according to step (a₁) or (a₂).

2. A process according to claim 1, comprising steps (a₁) and (b).

3. A process according to claim 1, wherein X is the radical of a mono-, di-, tri- or tetrasaccharide.

4. A process according to claim 3, wherein X is the radical of a galactose, lactose mannose, N-acetyl glucosamine, N-acetyl galactosamine or N-acetyl lactosamine.

5. A process according to claim 1, wherein R is linear or branched C₂-C₂₄-alkylene, which may be interrupted by -O- or -NR₃-, and R₃ is hydrogen or C₁-C₄-alkyl.

6. A process according to claim 1, wherein Y is a group -C(O)O-, -OC(O)-, -C(O)NR₄-, -NR₄C(O)-, -OC(O)-NH-, -NHC(S)NH- or -NHC(O)NH-, and R₄ is hydrogen or C₁-C₄-alkyl.

7. A process according to claim 1, wherein R₁ is fluorine and n is an integer from 0 to 4.

8. A process according to claim 1, wherein Q is a radical of formula (2a), and R₂ is trifluoromethyl.

9. A process according to claim 1, wherein in step (b) the carbohydrate(s) are attached to the radicals X by means of a glycosyl transferase or a mixture of different glycosyl transferases.

10. A process according to claim 1, wherein a monosaccharide or a mixture of different monosaccharides or a derivative thereof is attached to the X radicals in step (b).

11. A process according to claim 1, wherein sialic acid is attached to the X radicals by means of a sialyl transferase in step (b).

16. A process according to claim 3, wherein X is the radical of a mono- or disaccharide.

17. A process according to claim 16, wherein X is the radical of a disaccharide.

18. A process according to claim 5, wherein R is linear C₄-C₁₈-alkylene.

19. A process according to claim 18, wherein R is linear C₆-C₁₀-alkylene.

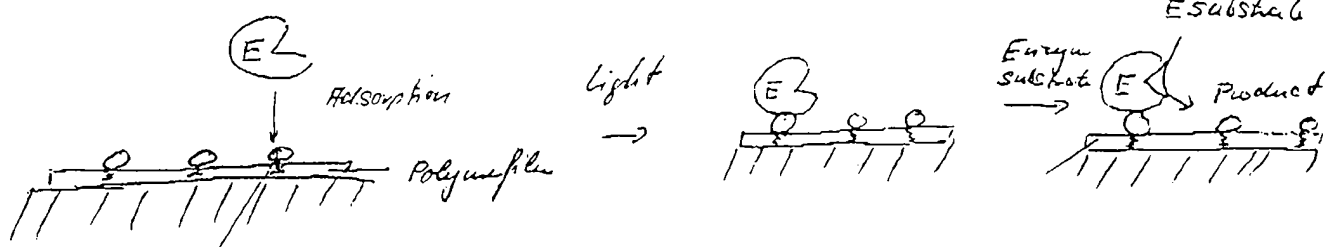
20. A process according to claim 7, wherein n is 0.

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Jan. 24, 2003

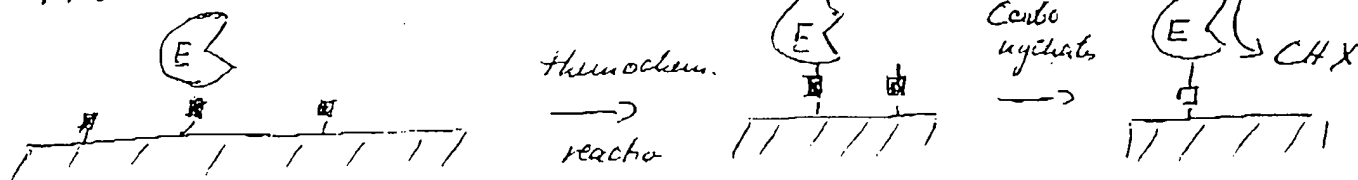
APPENDIX B

1) Myasaka



photoactive
reagent, adsorbed to
the polymer film
E = Enzyme

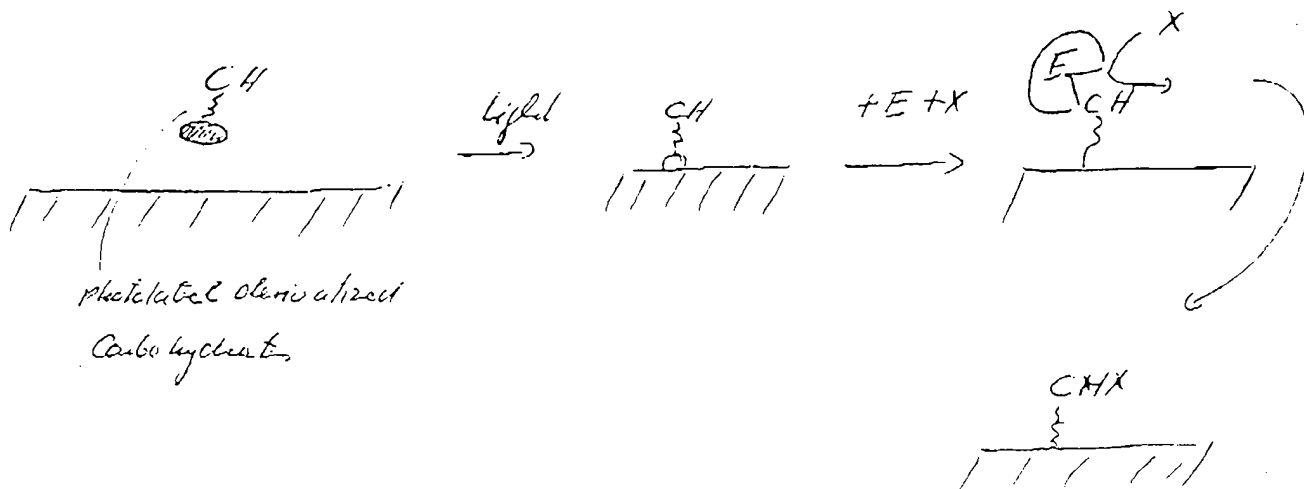
2) Mazid



X = Reactive function

E = Enzyme that modifies
Carbohydrates

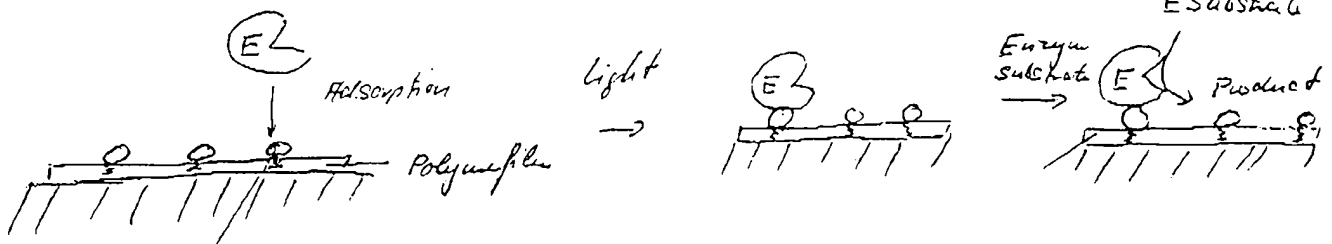
3) CSEM



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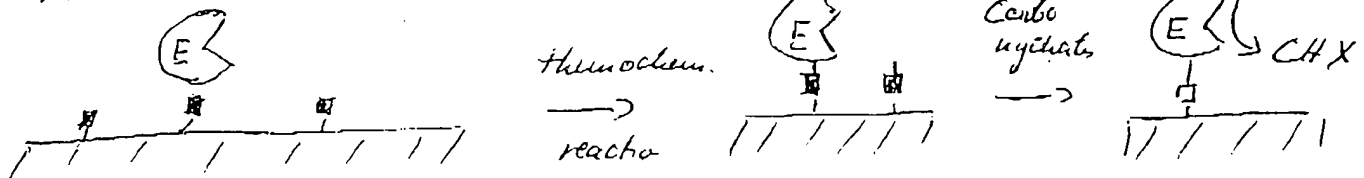
Jan. 24, 2003

1) Miyasaka



photoactive reagent, adsorbed to the polymer film
E = Enzyme

2) Mazid



X = Reactive function
E = Enzyme that modifies Carbohydrates

3) CSEM

